General

Guideline Title

Everolimus for preventing organ rejection in liver transplantation.

Bibliographic Source(s)

National Institute for Health and Care Excellence (NICE). Everolimus for preventing organ rejection in liver transplantation. London (UK): National Institute for Health and Care Excellence (NICE); 2015 Jul 22. 49 p. (Technology appraisal guidance; no. 348).

Guideline Status

This is the current release of the guideline.

This guideline meets NGC's 2013 (revised) inclusion criteria.

Recommendations

Major Recommendations

Everolimus (EVR) is not recommended within its marketing authorisation for preventing organ rejection in people having a liver transplant.

People whose treatment with EVR was started within the National Health Service (NHS) before this guidance was published, should be able to continue EVR until they and their NHS clinician consider it appropriate to stop.

Clinical Algorithm(s)

None provided

Scope

Disease/Condition(s)

Organ rejection in liver transplantation

Guideline Category

Assessment of Therapeutic Effectiveness

Prevention

Treatment

Clinical Specialty

Gastroenterology

Internal Medicine

Nephrology

Surgery

Intended Users

Advanced Practice Nurses

Nurses

Physician Assistants

Physicians

Guideline Objective(s)

To assess the clinical effectiveness and cost-effectiveness of everolimus (EVR) for preventing organ rejection in liver transplantation

Target Population

Adults on maintenance immunosuppressive therapy following allogeneic liver transplantation

Interventions and Practices Considered

Everolimus (EVR) (not recommended for preventing organ rejection in liver transplant)

Major Outcomes Considered

- Clinical effectiveness
  - Patient survival
  - Graft survival
  - Time to acute rejection
  - Time to recurrence of hepatocellular carcinoma
  - Renal function
  - Time to end-stage renal disease
  - Adverse effects of treatment
  - Health-related quality of life (HRQL)
- Cost effectiveness

Methodology

Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Primary Sources)

Hand-searches of Published Literature (Secondary Sources)

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

Note from the National Guideline Clearinghouse (NGC): The National Institute for Health and Care Excellence (NICE) commissioned an independent academic centre to perform an assessment of the manufacturer's submission on the technology considered in this appraisal and prepare an Evidence Review Group (ERG) report. The ERG report for this appraisal was prepared by Matrix and Peninsula Technology Assessment Group (PenTAG) (see the "Availability of Companion Documents" field).

Clinical Effectiveness

Description of Company's Search Strategy and Comment on Whether the Search Strategy Was Appropriate

Clinical Effectiveness Searches

The company ran four systematic literature reviews in order to identify relevant published and unpublished clinical data. These targeted:

1. Clinical data for the intervention of interest, everolimus (EVR) + reduced dose tacrolimus (rTAC)
2. Studies suitable for a network meta-analysis (NMA), both for the intervention and the two comparator regimens (azathioprine [AZA] + TAC and mycophenolate mofetil [MMF] + TAC) with or without corticosteroids
3. Non-randomised controlled trial (RCT) data for the intervention of interest, EVR + rTAC
4. Adverse event (AE) data

The search strategy was last updated in August 2014, so the results are considered current for this submission. The effectiveness search syntax took the following form:

(Terms for liver transplant or hepatic transplantation or graft) AND (terms for Everolimus (including brand names Certican or Zortress)) OR (terms for Azathioprine) OR (terms for mycophenolic acid) AND (terms for cyclosporine) OR (terms for tacrolimus).

The company searched all of the required bibliographic databases, in addition to clinical trial registries and conference proceedings. The ERG is content with the range of resources used in this submission and, therefore, the company's attempts to locate published and unpublished RCT evidence.

The ERG points to the following limitations of the searches undertaken:

The search returns are limited to studies that use cyclosporine or TAC in combination with EVR or AZA or MMF. Any studies that evaluate the efficacy of EVR as a stand-alone intervention, would be missed by this search. However, the expected license for EVR in liver transplantation was only in combination with rTAC, any studies which might be useful for parametrisation of the model (for example) would be missed.

The bibliographic searches were date limited 1990-current and the conference proceedings were date limited 2012-current.

The ERG noticed a small typographical error in the clinical effectiveness searches. The Boolean connector OR had been inadvertently omitted between mycophenolic acid/morpholinoethyl ester.

After clarification, the company provided the ERG with a list of the 7 unique studies resulting from correcting this error. These studies were double-screened and all 7 studies were excluded. The ERG is content that this point has been dealt with satisfactorily.

Adverse Events

The company used their clinical effectiveness search strategy to identify studies reporting adverse events. This strategy worked as the company did not limit their clinical effectiveness searches by study design (i.e., to RCTs using an RCT search filter). The ERG is happy to accept these searches.

Statement of the Inclusion/Exclusion Criteria Used in the Study Selection and Comment on whether They Were Appropriate

As previously mentioned, Novartis presented four systematic literature reviews to identify relevant published and unpublished clinical data. The inclusion/exclusion criteria in the table below were used in the search of RCT studies. The eligibility criteria for the NMA studies is similar to the one presented in the table below. The company reported that none of the search strategies for non-RCTs or adverse events retrieved any relevant studies. Text in bold presents additional information provided to the ERG by the company upon request for clarification.

Eligibility Criteria Used in the Search for RCTs

Criteria	Inclusion Criteria	Exclusion Criteria
Population	Adults on maintenance immunosuppressive therapy following allogeneic liver transplantation	• Any non-liver related transplant patients • Pre-liver transplant patients including induction therapy • Non-human • Paediatric
Intervention/Comparators	EVR in combination with rTAC with or without corticosteroids AZA or MMF in combination with a calcineurin inhibitor (CIC or TAC) with or without corticosteroids	• Sirolimus regimens • Any regimen in combination with an induction treatment • Any study without information on dosages
Outcomes	• Patient survival • Graft survival • Time to acute rejection • Time to recurrence of hepatocellular carcinoma • Renal function • Time to end-stage renal disease • Adverse effects of treatment • HRQL	• Studies that do not focus on rejection of the liver as an outcome (efficacy) or HRQL • Studies with only cost and no clinical outcomes
Study Design	• RCTs of any duration, including cross-over RCTs if data were presented at cross-over • Studies published as abstracts or conference presentations were eligible for the primary analysis of clinical effectiveness if adequate data are provided.	Non-RCT study designs or articles reporting results of RCTs published elsewhere, e.g., reviews, meta-analyses/pooled analyses, editorials, notes, comments or letters

Abbreviations: AZA, azathioprine; CIC, ciclosporin; EVR, everolimus; HRQL, health-related quality of life; MMF, mycophenolate mofetil; RCT, randomised controlled trial; rTAC, reduced dose tacrolimus; TAC, tacrolimus

Refer to the original guideline document for information on justification of inclusion/exclusion criteria.

To note is that for the network meta-analysis (NMA) the company decided to develop a refined criteria as to include any study that included two or more of the following comparators within the study:

1. EVR plus rTAC with or without a corticosteroid
2. Any combination of MMF and a calcineurin inhibitor (reduced/standard ciclosporin [CIC] or reduced/standard dose TAC monotherapy) with or without a corticosteroid
3. Any combination of AZA and a calcineurin inhibitor (reduced/standard dose CIC or reduced/standard dose TAC monotherapy) with or without a corticosteroid
4. TAC monotherapy with or without corticosteroid

The scope defined the intervention as EVR in combination with TAC and a corticosteroid, however the decision problem addressed in the submission looked at the use of EVR + rTAC with or without corticosteroids. The specification of reduced TAC seems appropriate in theory as the indication of EVR is in combination with rTAC. However, the rTAC in the H2304 study is the equivalent to a standard dose of TAC in UK practice.

Overall, the inclusion criteria seem appropriate to identify all the relevant evidence set out in the NICE scope.

Studies Included and Excluded

The search strategy identified one RCT, H2304, which studied the intervention of interest (EVR + rTAC with or without corticosteroids) and 33 individual records which were related to this RCT.

A brief description of the studies excluded and reasons for exclusion are presented in Table 5 of the ERG report.

Economic Evaluation

Description of Company's Search Strategy and Comment on Whether the Search Strategy Was Appropriate

Following satisfactory answers to questions raised in clarification, the ERG is content to accept the cost-effectiveness searches run by the company.

The search strategy takes the following form, and it was last updated in August 2014, so the results are considered current for this submission:

(Terms for liver transplant or hepatic transplant or graft) AND (terms for Everolimus) AND (a standard economics/costs search filter).

The company searched all of the required resources for this section of the submission.

The ERG point to the following limitations identified on the searches undertaken:

The company, following clinical advice, used a date limit on their cost-effectiveness searches of 1990-current.

Search Results

A range of studies were identified and their relevance assessed according to the inclusion/exclusion criteria described in the company's submission.

While at the primary review the majority of the studies failed to meet the inclusion criteria, at the secondary review, no studies met the inclusion criteria. Therefore, no relevant cost-effectiveness studies were found. For this reason, a *de novo* analysis was undertaken.

Number of Source Documents

Clinical Effectiveness

Only one randomised controlled trial (RCT) and 33 records related to this RCT were included in the review.

Economic Evaluation

- No relevant cost-effectiveness studies were found.
- The manufacturer submitted a *de novo* economic model.

Methods Used to Assess the Quality and Strength of the Evidence

Expert Consensus

Rating Scheme for the Strength of the Evidence

Not applicable

Methods Used to Analyze the Evidence

Meta-Analysis

Review of Published Meta-Analyses

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

Note from the National Guideline Clearinghouse (NGC): The National Institute for Health and Care Excellence (NICE) commissioned an independent academic centre to perform an assessment of the manufacturer's submission on the technology considered in this appraisal and prepare an Evidence Review Group (ERG) report. The ERG report for this appraisal was prepared by Matrix and Peninsula Technology Assessment Group (PenTAG) (see the "Availability of Companion Documents" field).

Clinical Effectiveness

Description and Critique of Company Approach to Validity Assessment

A critique of the company's approach to the analysis of relevant randomised controlled trials (RCTs) is provided in the Table 6 of the ERG report alongside comments made by the ERG on its appropriateness.

The company has covered the elements used in the critical appraisal of RCTs according to the Centre for Reviews and Dissemination Systematic Reviews checklist (2008). Additionally, the ERG notes that a limited number of UK patients were involved in the trial. The study was conducted predominantly with patients in the US.

The company assessed the network meta-analysis (NMA) studies for their validity. Even though they follow the template suggested by the National Institute for Health and Care Excellence (NICE) to assess the NMA studies, the ERG does not find that it provides very useful information as all the questions were answered with a Yes/No/Unclear reply. So for example, one of the criteria used by the company to assess the validity of the trials is "Were the groups similar at the outset of the study in terms of prognostic factors?" If the company considered this to be a "Yes", there is no way for the ERG to assess this answer as the submission does not state the criteria used to assess similarity in terms of prognostic factors.

Also the proportion of answers answered with "unclear" was considerably large. For example, for the first NMA question, "Was randomisation carried out appropriately?" 68% of the answers were answered "unclear". Overall for all questions answered, 40% were answered "Unclear".

Studies were also grouped into categories within the critical appraisal section, so it was difficult to assess how each study had been individually appraised.

Network Meta-analysis

Twenty-two RCTs were included in the review to enable a network of studies. The following comparator arms were found:

- Everolimus plus reduced dose tacrolimus (EVR + rTAC)
- Mycophenolate mofetil plus standard dose tacrolimus (MMF + TAC)
- Mycophenolate mofetil plus reduced dose tacrolimus (MMF + rTAC)
- Mycophenolate mofetil plus standard dose ciclosporin (MMF + CIC)
- Azathioprine plus standard dose tacrolimus (AZA + TAC)
- Azathioprine plus standard dose ciclosporin (AZA + CIC)
- Standard dose tacrolimus (TAC)

After selecting the relevant clinical studies, the company conducted a feasibility assessment of the NMA, which was based on 16 clinical endpoints extracted from the studies. Table 7 of the ERG report highlights the 16 efficacy and safety endpoints chosen.

Due to a wide range of studies considered for the NMA and time constraints, the ERG approach was to focus on:

- The studies included in the final NMA
- The studies used to derive the parameters included in the economic model (treated biopsy proven acute rejection [tBPAR] and renal functioning)

Nevertheless, the ERG is still not clear which studies have been included in the final NMA analysis for the biopsy proven acute rejection (tBPAR) outcome, due to lack of clarity and transparency in the submission.

Refer to Section 4 of the ERG report for more information on clinical effectiveness analysis.

Economic Evaluation

Model Structure

The company's cost-effectiveness model was developed as a patient simulation model. The structure of the economic model (see Figure 8 of the ERG report) includes a core hepatic model and a renal sub-model and is reported to be appropriate and reflective of the clinical pathway of immunosuppression therapy after liver transplantation.

The company states that the use of a patient simulation model is in line with the Decision Support Unit (DSU) technical support document recommendations as the technical report suggests this modelling approach is appropriate when the patient flow is determined by time since last event or history of previous event.

The company also explains that the decision to capture the renal sparing effect associated with EVR + rTAC (demonstrated in the H2304 trial) through a renal sub-model *was considered important because the treatment effect* [survival of liver graft] *has an impact on more than one aspect of a patients' health*. Additionally it is mentioned that *International Society for Pharmacoeconomics and Outcomes Research (ISPOR) good research practice guidelines encourage the design option of using sub-models to simplify the model structure*.

Furthermore, the company reports that a patient level simulation approach facilitates *between-model calculations* involving the hepatic core model and the renal sub-model. However it adds that *in the patient simulation, events that occur in the core* [hepatic] *model do not impact on progression through the renal sub-model. The exception to this is death, which can occur as a result of progression in either model, and is considered an absorbing state in both models*.

Health states considered in the hepatic core model along with their brief description are provided in Table 20 of the ERG report, and health states of renal sub-model are presented in Table 21 of the ERG report.

The cycle length in the economic model is 3 months and a half-cycle correction was not applied. The company justifies the choice of cycle length with clinical expert opinion which stated that *most acute rejection occurs after 3 months post transplantation*. The time horizon considered in the economic model was lifetime (the model was run for 320 cycles - 80 years).

Model Validation

It is stated by the company that the model was checked for internal quality with regards to formulae, programming string and data inputs, however the ERG discovered several important logic errors and formulae in the economic model sent by the company. Data inputs also presented inconsistencies when compared with values reported in the submission.

Model outputs have not been externally validated. This means that life expectancy, graft loss and renal function weren't compared with any available literature. Whenever possible, the ERG tried to validate model main outcomes with external sources.

Refer to Sections 5, 6 and 7 of the ERG report (see the "Availability of Companion Documents" field) for additional information on the company's economic evaluation and ERG critique of the approach used by the company.

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

Considerations

Technology appraisal recommendations are based on a review of clinical and economic evidence.

Technology Appraisal Process

The National Institute for Health and Care Excellence (NICE) invites 'consultee' and 'commentator' organisations to take part in the appraisal process. Consultee organisations include national groups representing patients and carers, the bodies representing health professionals, and the manufacturers of the technology under review. Consultees are invited to submit evidence during the appraisal and to comment on the appraisal documents.

Commentator organisations include manufacturers of the products with which the technology is being compared, the National Health Service (NHS) Quality Improvement Scotland and research groups working in the area. They can comment on the evidence and other documents but are not asked to submit evidence themselves.

NICE then commissions an independent academic centre to review published evidence on the technology and prepare an 'assessment report'. Consultees and commentators are invited to comment on the report. The assessment report and the comments on it are then drawn together in a document called the evaluation report.

An independent Appraisal Committee then considers the evaluation report. It holds a meeting where it hears direct, spoken evidence from nominated clinical experts, patients and carers. The Committee uses all the evidence to make its first recommendations, in a document called the Appraisal Consultation Document (ACD). NICE sends all the consultees and commentators a copy of this document and posts it on the NICE Web site. Further comments are invited from everyone taking part.

When the Committee meets again it considers any comments submitted on the ACD; then it prepares its final recommendations in a document called the Final Appraisal Determination (FAD). This is submitted to NICE for approval.

Consultees have a chance to appeal against the final recommendations in the FAD. If there are no appeals, the final recommendations become the basis of the guidance that NICE issues.

Who Is on the Appraisal Committee?

NICE technology appraisal recommendations are prepared by an independent committee. This includes health professionals working in the NHS and people who are familiar with the issues affecting patients and carers. Although the Appraisal Committee seeks the views of organisations representing health professionals, patients, carers, manufacturers and government, its advice is independent of any vested interests.

Rating Scheme for the Strength of the Recommendations

Not applicable

Cost Analysis

Summary of Appraisal Committee's Key Conclusions

Availability and Nature of Evidence

The Committee concluded that the choice of 2 separate models and the way in which they had been constructed was not necessarily the most appropriate approach to the economic evaluation.

The Committee agreed that the considerable uncertainty in the results of the network meta-analysis (NMA), related to the lack of clarity and transparency in the company's submission and inconsistency across studies with respect to tacrolimus (TAC) trough levels, significantly undermined the reliability of the model. The Committee concluded that the changes made by the company in the new base case did not address the lack of clarity and transparency in the company's original submission, and did not address some fundamental concerns about the reliability of the model.

Uncertainties Around and Plausibility of Assumptions and Inputs in the Economic Model

The Committee was cautious about the robustness of the incremental cost-effectiveness ratios (ICERs) because of uncertainty around:

- Efficacy estimates from the NMA
- The utility estimates for some of the health states were not based on robust evidence

Incorporation of Health-related Quality-of-Life Benefits and Utility Values. Have Any Potential Significant and Substantial Health-related Benefits Been Identified That Were Not Included in the Economic Model, and How Have They Been Considered?

The Committee acknowledged the comments from the company that the best available literature sources were used for each of the health states but it did not accept that the evidence for some of the values used was robust.

The Committee agreed that everolimus (EVR) was innovative in its potential to preserve renal function but it could not identify any substantial health benefits that had not been captured in the quality-adjusted life year (QALY) estimates in the modelling.

Are There Specific Groups of People for Whom the Technology Is Particularly Cost Effective?

None were identified by the Committee.

What Are the Key Drivers of Cost-effectiveness?

No key drivers were identified by the Committee. The Evidence Review Group (ERG) commented that it was not possible to identify the key drivers because the company did not undertake deterministic sensitivity analysis.

Most Likely Cost-effectiveness Estimate (Given as an ICER)

The Committee concluded that the ICERs for EVR with reduced-dose tacrolimus (rTAC) were unlikely to be lower than the company's estimates of £184,000 per QALY gained compared with the mycophenolate mofetil treatment (MMF) regimen and £107,600 per QALY gained compared with the azathioprine treatment regimen.

Method of Guideline Validation

External Peer Review

Description of Method of Guideline Validation

Consultee organisations from the following groups were invited to comment on the draft scope, Assessment Report and the Appraisal Consultation Document (ACD) and were provided with the opportunity to appeal against the Final Appraisal Determination (FAD).

- Manufacturer/sponsors
- Professional/specialist and patient/carer groups
- Commentator organisations (without the right of appeal)

In addition, individuals selected from clinical expert and patient advocate nominations from the professional/specialist and patient/carer groups were also invited to comment on the ACD.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of evidence supporting the recommendations is not specifically stated.

The Appraisal Committee considered clinical and cost-effectiveness evidence submitted by the manufacturer of everolimus (EVR) and a review of this submission by the Evidence Review Group (ERG). The main clinical effectiveness evidence came from one randomised controlled trial (RCT). For cost-effectiveness, the Appraisal Committee considered an economic model submitted by the manufacturer.

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

Appropriate recommendation for the use of everolimus (EVR) for preventing organ rejection in liver transplantation

Potential Harms

The summary of product characteristics states that for people who have had a liver transplant, exposure to tacrolimus (TAC) should be reduced to minimise calcineurin-related renal toxicity. The TAC dose should be reduced starting approximately 3 weeks after initiating administration together with everolimus (EVR), based on targeted TAC blood trough levels of 3 to 5 ng/ml. The summary of product characteristics for EVR lists the most common adverse reactions as infections, anaemia, hyperlipidaemia, new onset of diabetes mellitus, insomnia, anxiety, headache, hypertension, cough, nausea, peripheral oedema and impaired healing.

For full details of adverse reactions see the summary of product characteristics.

Contraindications

Contraindications

For full details of contraindications, see the summary of product characteristics.

Qualifying Statements

Qualifying Statements

- This guidance represents the views of the National Institute for Health and Care Excellence (NICE) and was arrived at after careful consideration of the evidence available. Healthcare professionals are expected to take it fully into account when exercising their clinical judgement. However, the guidance does not override the individual responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.
- Implementation of this guidance is the responsibility of local commissioners and/or providers. Commissioners and providers are reminded that it is their responsibility to implement the guidance, in their local context, in light of their duties to have due regard to the need to eliminate unlawful discrimination, advance equality of opportunity and foster good relations. Nothing in this guidance should be interpreted in a way that would be inconsistent with compliance with those duties.

Implementation of the Guideline

Description of Implementation Strategy

The Welsh Assembly Minister for Health and Social Services has issued directions to the National Health Service (NHS) in Wales on implementing National Institute for Health and Care Excellence (NICE) technology appraisal guidance. When a NICE technology appraisal recommends the use of a drug or treatment, or other technology, the NHS in Wales must usually provide funding and resources for it within 3 months of the guidance published.

Implementation Tools

Mobile Device Resources

Patient Resources

Resources

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Living with Illness

Staying Healthy

IOM Domain

Effectiveness

Patient-centeredness

Identifying Information and Availability

Bibliographic Source(s)

National Institute for Health and Care Excellence (NICE). Everolimus for preventing organ rejection in liver transplantation. London (UK): National Institute for Health and Care Excellence (NICE); 2015 Jul 22. 49 p. (Technology appraisal guidance; no. 348).

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2015 Jul 22

Guideline Developer(s)

National Institute for Health and Care Excellence (NICE) - National Government Agency [Non-U.S.]

Source(s) of Funding

National Institute for Health and Care Excellence (NICE)

Guideline Committee

Appraisal Committee

Composition of Group That Authored the Guideline

Committee Members: Dr Jane Adam (*Chair*), Department of Diagnostic Radiology, St George's Hospital, London; Professor Iain Squire (*Vice-chair*), Consultant Physician, University Hospitals of Leicester; Dr Graham Ash, Consultant in General Adult Psychiatry, Lancashire Care NHS Foundation Trust; Dr Jeremy Braybrooke, Consultant Medical Oncologist, University Hospitals Bristol NHS Foundation Trust; Dr Gerardine Bryant, General Practitioner, Swadlincote, Derbyshire; Professor Aileen Clarke, Professor of Public Health and Health Services Research, University of Warwick; Dr Andrew England, Senior Lecturer, Directorate of Radiography, University of Salford; Mr Adrian Griffin, Vice President, HTA & International Policy, Johnson & Johnson; Dr Ian Lewin, Honorary Consultant Physician and Endocrinologist, North Devon District Hospital; Ms Pamela Rees, Lay Member; Dr Paul Robinson, Medical Director, Merck Sharp & Dohme; Ms Ellen Rule, Director of Transformation and Service Redesign, Gloucestershire Clinical Commissioning Group; Dr Brian Shine, Consultant Chemical Pathologist, John Radcliffe Hospital, Oxford; Dr Peter Sims, GP, Devon; Dr Eldon Spackman, Research Fellow, Centre for Health Economics, University of York; Mr David Thomson, Lay Member; Dr John Watkins, Clinical Senior Lecturer, Cardiff University; Consultant in Public Health Medicine, National Public Health Service Wales; Professor Olivia Wu, Professor of Health Technology Assessment, University of Glasgow

Financial Disclosures/Conflicts of Interest

Committee members are asked to declare any interests in the technology to be appraised. If it is considered there is a conflict of interest, the member is excluded from participating further in that appraisal.

Guideline Status

This is the current release of the guideline.

This guideline meets NGC's 2013 (revised) inclusion criteria.

Guideline Availability

Available from the National Institute for Health and Care Excellence (NICE) Web site.

Availability of Companion Documents

The following are available:

- Everolimus for preventing organ rejection in liver transplantation. Costing statement. London (UK): National Institute for Health and Care Excellence (NICE); 2015 Jul. 1 p. (Technology appraisal guidance; no. 348). Available from the National Institute for Health and Care Excellence (NICE) Web site.
- Bacelar M, Nakum M, Durand A, Cooper C, Mujica-Mota R, Hyde C, Latimer N, Peters J. Everolimus (Certican®) for preventing organ rejection in liver transplantation. Single technology appraisal. NIHR HTA Programme. United Kingdom: Matrix Knowledge, Peninsula Technology Assessment Group (PenTAG); 2014 Nov. 144 p. Available from the NICE Web site.
- Bacelar M, Nakum M, Durand A, Cooper C, Mujica-Mota R, Hyde C, Latimer N, Peters J. Everolimus (Certican®) for preventing organ rejection in liver transplantation. Single technology appraisal. NIHR HTA Programme. Erratum. United Kingdom: Matrix Knowledge, Peninsula Technology Assessment Group (PenTAG); 2015 Jan. 35 p. Available from the NICE Web site.

Patient Resources

The following is available:

- Everolimus for preventing organ rejection in liver transplantation. Information for the public. London (UK): National Institute for Health and Care Excellence (NICE); 2015 Jul. 2 p. (Technology appraisal guidance; no. 348). Available from the National Institute for Health and Care Excellence (NICE) Web site. Also available for download in ePub and eBook formats from the NICE Web site.

Please note: This patient information is intended to provide health professionals with information to share with their patients to help them better understand their health and their diagnosed disorders. By providing access to this patient information, it is not the intention of NGC to provide specific medical advice for particular patients. Rather we urge patients and their representatives to review this material and then to consult with a licensed health professional for evaluation of treatment options suitable for them as well as for diagnosis and answers to their personal medical questions. This patient information has been derived and prepared from a guideline for health care professionals included on NGC by the authors or publishers of that original guideline. The patient information is not reviewed by NGC to establish whether or not it accurately reflects the original guideline's content.

NGC Status

This NGC summary was completed by ECRI Institute on November 20, 2015.

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